ABSTRACT OF THE DISCLOSURE

The phospholipid growth factor lysophosphatidic acids (LPAs) containing unsaturated fatty acids (18:1, 18:2 and 20:4) and fatty alcohols containing hydrocarbon chains with more than 4 carbons were capable of inducing a rapid formation of neointima, an initial step in the development of atherosclerotic plaque. LPAs with saturated fatty acids did not induce neointima formation. A Peroxisome Proliferator-Activated Receptors gamma (PPARγ)-specific agonist Rosiglitasone also induced a profound formation of neointima. GW9662, a selective and irreversible antagonist of PPARγ, abolished LPA- and Rosiglitazone-induced neointima formation, indicating that LPA-induced neointima formation requires the activation of PPARγ. These data suggest that LPA analogs that bind to but do not activate downstream signaling of PPARγ or antagonists of PPARγ that inhibit PPARγ signaling would be useful in the prevention and/or treatment of neointima formation and atherosclerosis.